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09/063,356	04/21/1998	KENNETH L. BEATTIE	029623/0109	4294

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EXAMINER
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SAUNDERS, DAVID A

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 02/26/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.	063356	Applicant(s)	BRETTIE
Examiner	SANDERS	Group Art Unit	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

### Status

- Responsive to communication(s) filed on 2/16/01 & 9/0/01.
- This action is **FINAL**.
- Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

### Disposition of Claims

- Claim(s) 21-82 is/are pending in the application.
- Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- Claim(s) 21, 25-26, 32-33, 37-39 is/are allowed.
- Claim(s) 22, 27-31, 34-36, 40-82 is/are rejected.
- Claim(s) 23-24 is/are objected to.
- Claim(s) \_\_\_\_\_ are subject to restriction or election requirement.

### Application Papers

- See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.
- The drawing(s) filed on 4/19/99 is/are objected to by the Examiner. APPROVED BY THE DRAFTSMAN
- The specification is objected to by the Examiner.
- The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. § 119 (a)-(d)

- Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- All  Some\*  None of the CERTIFIED copies of the priority documents have been received.
- received in Application No. (Series Code/Serial Number) \_\_\_\_\_.
- received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

### Attachment(s)

- Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_  Interview Summary, PTO-413
- Notice of Reference(s) Cited, PTO-892  Notice of Informal Patent Application, PTO-152
- Notice of Draftsperson's Patent Drawing Review, PTO-948  Other \_\_\_\_\_

## Office Action Summary

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The request filed on 9/10/01 (Paper 20) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/063,356 is acceptable and a CPA has been established. An action on the CPA follows.

In accord with notations in the advisory action mailed 3/13/01 (Paper 17), the amendment of 2/16/01 (Paper 16) has been entered in the record. Claims 21-82 are pending and under examination.

As set forth in the advisory action mailed 11/09/00 (Paper 15) all prior art rejections based on Degen et al. have been withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Upon further consideration of applicants arguments in paper 16, the rejection of record under 112, first paragraph are maintained below.

Claims 22, 27-31, 35-36, and 40-82 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims contain new matter.

Claim 27 contains new matter by reciting "about 0.33 micrometers to about 10 micrometers" page 14, line 10 recites "33 nm" (0.33 micrometer) without "about". Further, "10-micron diameter" (page 13, line 7) does not support "about 10". The examiner does, however,

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concur that these two portions of the disclosure, when taken together, reasonably support the diameter range recited in claim 27, except for the recitations of “about”.

Claim 28 contains new matter by reciting “about 0.45 micrometers to about 10 micrometers”. Page 15, line 3 recites 450 nm (0.45 micrometer) without “about”. As noted supra with respect to claim 27, there is no support for “about 10”.

In claims 29, 50 and 72 the recitations of “about”, at each end of the recited range of cross section areas, are unsupported.

In claim 30, about “1000 um” is not supported. Page 16 line 9 gives an upper range of the thickness as “up to 1 mm” --i.e., “up to 1000 um”. Recitation of “about 1000 um” is broader and thus unsupported.

In claims 31, 51 and 73 the recited range of channel inner surface area is without support. Applicant is relying upon the 33 nm lower dimension disclosed at page 14, line 10 and the 10 um upper dimension disclosed at page 13, line 7 for the range of diameters. Applicant is also relying upon the “about 100 um lower dimension disclosed at page 8, line 15 and the 1 mm upper dimension disclosed at page 16 line 9 for the range of thickness. No “about” is recited except at page 8, line 15. While these dimensions are consistent with the inner surface area range recited (without “about”) in claims 31, 51 and 73, the description of an apparatus feature in terms of inner surface area was not originally conveyed to the reader.

It is noted that any value of an inner surface area can result from multiplying an infinitude of circumferences by a infinitude of lengths. Therefore these claims encompass channels having

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diameters and lengths different from those pointed out by applicant and never recited in the disclosure.

With respect to claims 34, 54 and 76 the values given at page 25, lines 16-20, do not support the two recitations of “about” in line 2 of these claims.

In claims 22, 35, 45 and 67 there is no support for “glass or silicon” other than “nanoporous” glass (e.g. page 8, line 9, page 13, line 9), “microporous glass” (e.g. page 1, lines 21-22; page 13, line 9) or “porous silicon” (e.g. page 1, line 22; page 17, line 14).

In claim 44, part A) the generically recited reagents for detecting expression of a gene are not supported. Given recitations at page 4, line 28 and page 12, line 27 these must be recited as “gene specific probes.” Furthermore, pages 4 and 12 refer to “hybridization ... to an array”, and what is exemplified in Example 11, shows an “array” of different cDNA probes applied to different groups of channels (page 32, lines 21+). Thus the limitations of claims 48 or 49 and also claim 61 would be required in claim 44. Additionally pages 4 and 12 refer to “hybridization of cellular mRNA”; thus the “binding target” contained in the sample (claim 44, line 2) must be limited to cellular mRNA.

In claim 59, which further defines the “binding targets” of the sample of claim 44, there is no disclosure support for reciting “RNA or cDNA”. Page 12, line 27 and Example 11 that embodies its teaching only disclose the sample as containing “cellular mRNA” (page 12, line 27) or “cytoplasmic RNA” (page 33, line 5), which is then further described as “expressed

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sequences" (page 33, line 12). What is in the sample is not cDNA. Example 11 shows cDNA as a gene specific probe (binding reagent) in the arrays of channels.

In claim 60 "polynucleotides" is new matter because it is broader than cDNA, which is what was disclosed in Example 11 as the binding reagent in the arrays of channels. Also cDNA would be what one of skill would have recognized as being the "gene-specific probe" that would bind to the "cellular mRNA" of page 12, line 27.

In claim 64 there is no support for the recitation of "between normal and mutated states of a cell or tissue" because the examiner fails to see how the disclosures of detection mutations fall under the rubric of detecting "gene expression".

In claim 66, part (A) there is no support for recitation of a generic "first binding reagent" and a generic "second binding reagent" for use in a method to detect "sequence variation".

Figure 5, and Example 10 are the only portion of the original disclosure that embody detection of a sequence variation (in the form of a mutation). These only disclosed DNA as the immobilized binding reagent (e.g. page 11, line 12 - page 12, line 24). Therein only hybridization was disclosed (this would be true even if RNA is the immobilized binding reagent); thus the claim must be limited to "hybridization", as recited in dependent claim 80.

Furthermore, since Figure 5 and Example 10 show different oligonucleotide binding reagents bound to different groups of channels, there is no support for the method of claim 66 without the limitation of claim 70.

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Due to applicant's amendment and/or urgings presented in Papers 10 and 16, the examiner has withdrawn the following 112 first paragraph rejections.

- 1) The rejection of claims 37, 35 and 77 reciting "label".
- 2) The rejection of claim 63, which now recites "different experimental conditions".

With respect to the 112, first paragraph rejections that have been maintained, the examiner notes the following in response to applicant's urgings.

- 1) The rejections pertaining to recitations of "about" in conjunction with various recited dimensions are proper. Each recitation of "about" has expanded the scope of what is claimed beyond that which was ipsi verbis described in the original disclosure.
- 2) With respect to the generic recitations of "glass" and "silicon", applicant has urged that the "Brief Description of the Drawings" at page 13 has generic recitations of such. If so the examiner cannot find where so. Further, even if there were a generic recitation of these at page 13, such recitation must be taken in the context of what the Figures themselves show, which is only a "micro" or "nano" dimensioned apparatus.

Applicant has further urged that the recited "glass" or "silicon" would need to be porous any way, in order for the test to work by virtue of the sample flowing into the channels. This argument is unconvincing because nothing in any of the independent claims requires that the sample specifically flow into the discrete channels by means of their inherent porosity.

- 3) Regarding the undue scope of the reagents recited in claim 44, applicant has urged that the apparatus has been disclosed as being useful for a variety of assays that involve

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immunochemical binding, ligand-receptor binding etc. and that one of skill would have recognized that agents for these other types of binding assays could be provided in the channels. This argument misses the point of the rejection. Applicant is claiming a method of "detecting expression of at least one gene" (preamble). Page 4, lines 27-28 and page 12, lines 26-27, and Example 11 set forth the only disclosure where "gene expression" is recited, and therein all that was disclosed was "hybridization of cellular mRNA to an array of gene-specific probes." This is how applicant's disclosure defined and exemplified an analysis of "gene expression". That one of skill might have realized one could do this by other types of binding reactions does not overcome. The fact is that applicant did not describe these in the context of "gene-expression".

4) Based upon his understanding that the term "binding targets" in claim 59 refers to what is being detected in the sample, the examiner has modified the previously stated rejection of claim 59 as to what is new matter and what would be acceptable. The examiner will thus not address applicant's traverse of the new matter rejection of claim 59.

5) Regarding claim 60, applicant has urged that the disclosure teaches various types of nucleic acid molecules including both oligonucleotides and polynucleotides as being immobilized in the channels (page 24, line 20). This traverse misses the point. The examiner does not deny that any of these various subgeneres of nucleic acids could be immobilized in the channels. The problem is that what was disclosed at page 24 was not in the context of evaluating "gene expression", as required by base claim 44. The examiner's statements pertaining to cDNA

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have been based upon what applicant has taught for a method of analyzing "gene expression" at page 12, line 27 and in Example 11.

6) With respect to claim 64 applicant has urged that page 32, lines 1-6 support this claim. However the examiner finds that these lines of page 32 appear in Example 10, not Example 1. It is the latter, not the former, Example which pertains to detecting "gene expression."

7) Regarding claim 66, applicant has not addressed the issues concerning the generic nature of the "first" and "second binding agent", nor has applicant urged why the method should not be limited to hybridization.

Applicant did traverse the requirement that the limitations of claim 70 be recited in claim 66. The traversal states, that one "would recognize that a mutation can be detected by applying different samples to two different groups of channels containing the same appropriate binding agent." This is unconvincing because applicant never specifically disclosed or even conveyed the general concept that multiple samples would be applied to one wafer substrate having multiple groups of channels. Rather, the disclosure teaches that one would flood the entire wafer with one sample (page 33, line 18).

Applicant's arguments filed 2/16/01 have been fully considered but they are not persuasive. For the reasons above, applicant has recited new claims which encompass embodiments not set forth at the time the application was originally filed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, Ph.D., whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday-Thursday from 8:00 a.m. to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

D. Saunders:jmr

February 11, 2003

*David A. Saunders*  
DAVID SAUNDERS  
PRIMARY EXAMINER  
ART UNIT 182-1644